Epigenomic annotation of enhancers predicts transcriptional regulators of human neural crest.

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Public Summary:

Scientific Abstract:
Neural crest cells (NCC) are a transient, embryonic cell population characterized by unusual migratory ability and developmental plasticity. To annotate and characterize cis-regulatory elements utilized by the human NCC, we coupled a hESC differentiation model with genome-wide profiling of histone modifications and of coactivator and transcription factor (TF) occupancy. Sequence analysis predicted major TFs binding at epigenomically annotated hNCC enhancers, including a master NC regulator, TFAP2A, and nuclear receptors NR2F1 and NR2F2. Although many TF binding events occur outside enhancers, sites coinciding with enhancer chromatin signatures show significantly higher sequence constraint, nucleosomal depletion, correlation with gene expression, and functional conservation in NCC isolated from chicken embryos. Simultaneous co-occupancy by TFAP2A and NR2F1/F2 is associated with permissive enhancer chromatin states, characterized by high levels of p300 and H3K27ac. Our results provide global insights into human NC chromatin landscapes and a rich resource for studies of craniofacial development and disease.